



Intraluminal Fibre-Tip Centring can Improve Endovenous Laser Ablation: A Histological Study

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Abstract *Objective:* In this histological study, the lateral saphenous vein of the goat was treated using a laser fibre to which a tulip-shaped, self-expandable catheter had been fixed to achieve endovenous laser ablation (EVLA). The catheter centres the laser fibre in the vein preventing direct contact with the vein wall. This study aims to establish whether prevention of direct contact between the fibre tip and the vein wall prevents ulceration and perforation of the vein wall and perivenous tissue destruction.

Materials and Methods: Ten lateral saphenous veins were treated, using the tulip catheter, in goats under general anaesthesia. Ten more veins were treated with a normal bare fibre. We used a 980 nm diode laser to provide the energy. Postoperatively the veins were removed immediately, at 10 days and after 3 weeks for histological examination. Destruction of the vessel wall was measured and perivenous tissue destruction was quantified using a graded scale.

Results: Ulceration and perforation were prevented when using the tulip catheter. It also achieved more even vein wall necrosis. Tulip-catheter-treated veins show a transmural vein wall necrosis in, on average, 80% of the total circumference compared to 64% in bare-fibre treated veins. Less perivenous tissue destruction was seen with the new catheter (perivenous tissue destruction scale: tulip catheter: 1.7 vs. bare fibre: 3.8). Three weeks after treatment, we found regression of the perivenous tissue destruction as the healing process continued.

Conclusions: EVLA using the tulip catheter avoids ulceration and perforation of the vein associated with treatment using a bare fibre. It also results in more even circumferential vein wall necrosis and less perivenous tissue destruction.

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Introduction

Endovenous laser ablation (EVLA) has become a popular minimally invasive alternative to surgical vein stripping in the treatment of saphenous vein reflux. By catheterising the saphenous vein and introducing a bare fibre into the lumen, light energy is delivered within the vein to achieve selective vein wall destruction. This energy is absorbed by blood and water or by the vein wall. The aim of this technique is completely to obliterate the incompetent vein irreversible. Although EVLA has fewer side effects than conventional saphenous femoral ligation and stripping^{1–5} resulting in fewer haematomas, less postoperative pain, paraesthesia and time off work, the technique still can be improved. Complications of EVLA include postoperative ecchymosis, pain, bruising and periphlebitis. These are due to vein wall perforation and energy dissemination in the perivenous tissue^{6,7} and probably arise when the laser fibre tip frequently contacts the vessel wall during treatment. This has been observed on ultrasound imaging.⁸ Tumescence anaesthesia induces spasm of the vein around the fibre and can diminish this effect, but does not eliminate the problem.

When energy is delivered, direct contact between the fibre tip and the vessel wall may result in ulceration or perforation of the vein.^{6,9–11} The tissue effects are achieved not only by direct absorption of the laser light, but also by convection of heat energy from the fibre tip into the surrounding tissue.^{12,13} Uneven energy application during treatment may also be the cause of a recanalisation.⁷ So if the laser fibre could be centred within the vein lumen, complications of EVLA may be minimised.

A new catheter fixed to the fibre was designed (Fig. 1). The tulip-shaped, self-expandable distal end at the fibre tip expands within the vein lumen and pushes the vein wall away. The shape of the self-expandable tip allows withdrawal from the fibre and catheter using the conventional EVLA procedure. This new catheter design was evaluated in an animal model.

Purpose

EVLA performed with an intraluminal fibre-tip centring device was evaluated in an experimental study in goats. This study was undertaken to answer the following question: Can avoidance of direct contact between the fibre tip and the vein wall prevent vessel wall ulceration, perforation and perivenous tissue destruction? Uniformity of vein wall destruction was compared in veins treated with a normal bare fibre and veins treated with the tulip catheter.

Materials and Methods

Materials and techniques

Our investigation was approved by the ethics committee for animal experiments at the Catholic University of Leuven, Belgium. Goat saphenous veins were used since the lateral saphenous vein has a mean diameter of 4–6 mm in the supine position, which is comparable to human veins (Fig. 2).

In 10 goats, 20 lateral saphenous veins were treated with EVLA. The goats were treated under general anaesthesia. Under ultrasound control (Terason t 3000 laptop ultrasound, Teratech, Burlington, USA) access was obtained by a puncture in the distal part of the lateral saphenous vein. A sheath was introduced and the fibre (600 μm) was placed near the saphenofemoral junction. Physiological saline (at 22 °C) was injected abundantly around the saphenous vein inducing spasm of the vein and acting as a protective barrier to the perivenous tissue. We injected, on average, 134 ml of liquid around the target veins, equivalent to 9.2 ml cm⁻¹. Ten veins were treated using a normal bare fibre (group 1), the remaining 10 using the new tulip-shaped, self-expandable catheter (group 2). Veins were treated with a 980 nm diode laser (Inter-Medic^o, Barcelona, Spain), using a continuous pullback protocol. Power was set to 8 W and pullback speed was adjusted to deliver a linear endovenous energy density (LEED)¹⁷ between 60 and 65 J cm⁻¹.

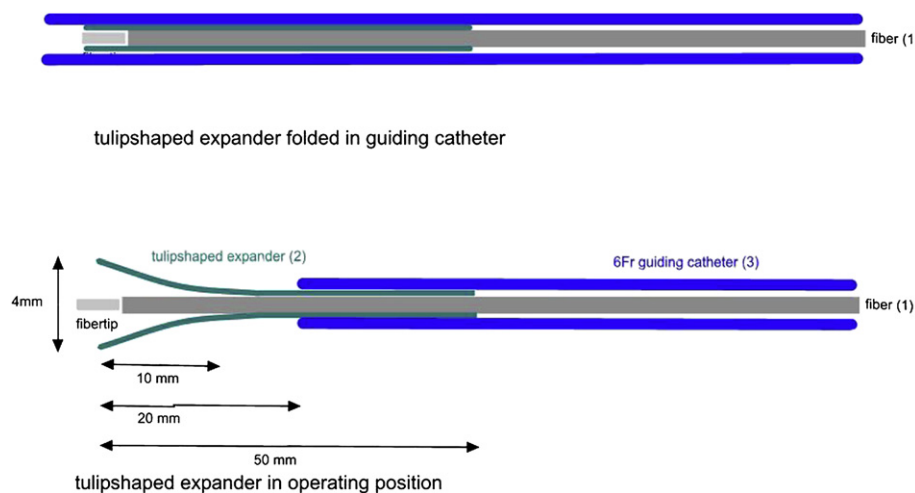


Figure 1 Tulip-shaped self-expandable catheter fixed to the fibre.

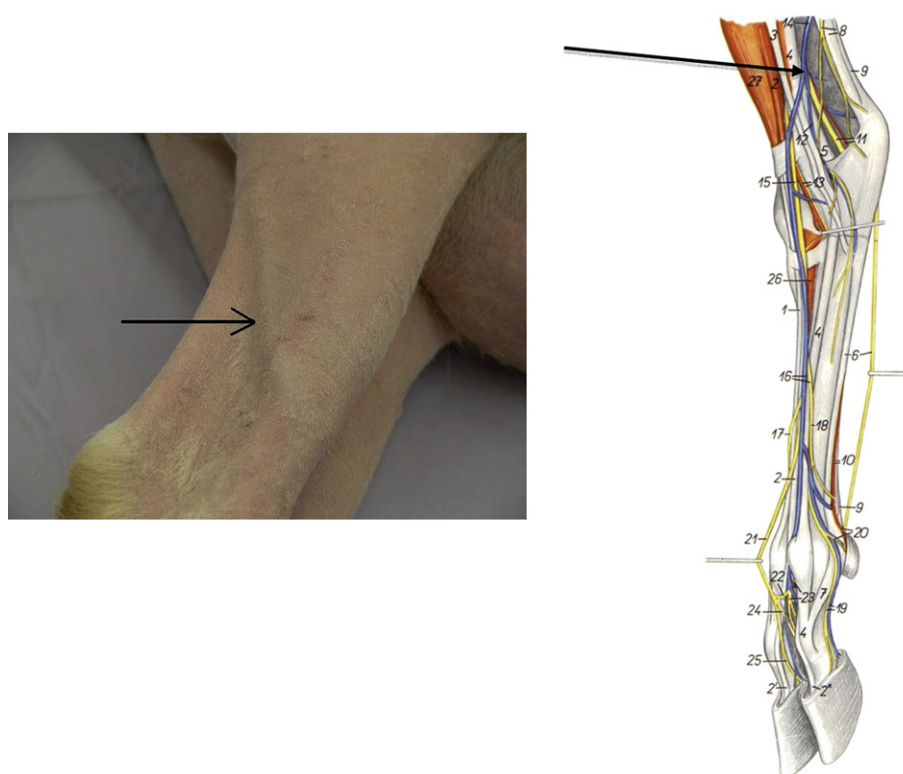


Figure 2 The lateral saphneous vein in a goat.

The mean length of the treated segment was 14.5 cm. Postoperatively, the veins were completely surgically removed, including perivenous tissue, at intervals following treatment. Six veins were removed immediately, eight veins after 10 days and six veins after 3 weeks. Excised veins were prepared for histological examination. About 11–15 sections of each of these veins were taken at random.

The pathologists measured the diameter and the depth of ulceration in the vein wall using a range of magnifications. Each optical field correlates with a constant defined diameter. Eyepiece graticules were used for measurement of the specimens. The perivenous tissue destruction was

quantified using a scoring system (Fig. 3) devised for this study, as described below.

Description of the fibre-tip catheter: tulip catheter

The fibre-tip centring catheter (Tobrix, Waalre, the Netherlands) consists of a hollow tube, fixed to the laser fibre. This tube has tulip-shaped, self-expandable blades at its distal end (around the fibre tip). The tube is folded into an outer guiding catheter, which permits easy access to the vein undergoing treatment. When the outer guiding catheter is withdrawn (pullback), the tulip-shaped blades at the distal end of this tube expand and push the vein wall

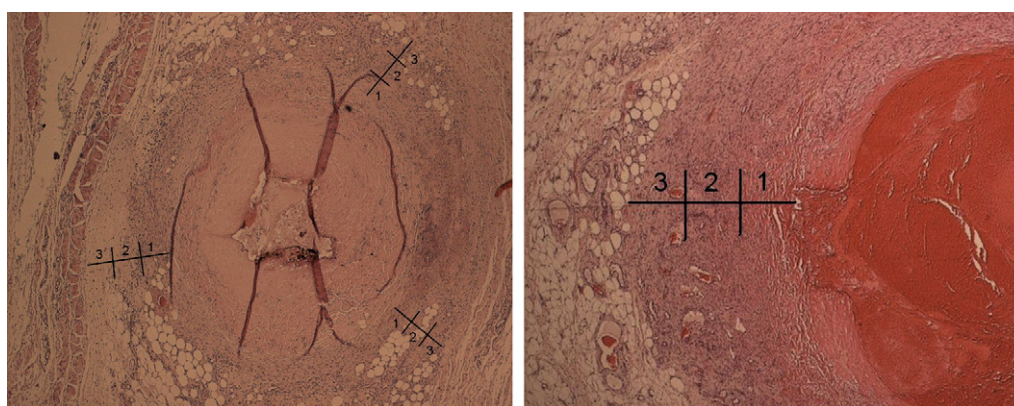


Figure 3 Perivenous tissue destruction scale: the perivenous destruction is measured at three points (A,B,C). The distance between the edge of the outer vein wall and the surrounding fascia is divided into three parts (1,2,3).

away. With this manoeuvre the fibre tip is centred intraluminally and prevents direct contact with the vein wall (Fig. 1).

The catheter is made from PEEK, an organic polymer, semi-crystalline thermoplastic, with a melting point around 343 °C (662 °F).¹⁴ It is highly resistant to thermal degradation as well as attack by both organic and aqueous environments. It is considered an advanced biomaterial used in medical implants.^{15,16} PEEK has excellent mechanical and chemical resistance properties that are retained to high temperatures. This catheter is referred to below as the tulip catheter.

Perivenous tissue destruction scale (Fig. 3)

The lateral saphenous vein in a goat is surrounded by a triangle-shaped fascia. At three different points at the edge of the vein, located 120° apart, the perivenous tissue destruction was measured. The distance between the vein wall and the surrounding fascia was divided into three equal layers. The extent of necrosis was graded following the scale: 0 = no necrosis, 1 = necrosis. Consequently, at each location, if the three layers were involved, the extent of necrosis was graded 3. Each part where necrosis is seen was scored 1. Consequently, if the necrosis was seen in all three positions, the maximum necrosis can reach a score equal to 9. Perivenous tissue destruction was measured immediately after treatment and then after 10 days and 3 weeks.

Measurements of perivenous temperature

The temperature in the perivenous fluid used to simulate tumescent anaesthesia was measured using thermocouples (thermocouple type K, Pronto tc, Thermo-Electric, Balen, Belgium). One needle was inserted at the proximal and another at the more distal part of the vein. The location of the needle in the perivenous liquid in the immediate proximity of the vein wall was checked by perioperative ultrasound. The thermocouples were connected to a digital thermometer (Pronto tc, Thermo-Electric, Balen, Belgium). Temperature was measured during fibre withdrawal to determine the maximum temperature for both the groups (with and without tulip catheter).

Statistical evaluation

Statistical analysis was performed using SPSS 16.0 (Statistical Package for the Social Sciences; SPSS Inc., Chicago, IL, USA). Inter-group variances for unpaired continuous and ordinal data were evaluated non-parametrically using the Student's *t*-test. An α -level of significance of 0.05 was used.

Results

Ten goats were treated according to the protocol described above. The mean diameter of the veins was 0.47 cm (SD: 0.08 cm) measured in the supine position. LEED was

Table 1 Histological data of veins immediately removed after treatment. Group 1: without catheter. Group 2: with tulip-catheter.

	none	ulceration	perforation	depth
Group 1 <i>n</i> = 3	<i>n</i> = 7	<i>n</i> = 7	<i>n</i> = 25	0.51 mm
Sections: 39				(SD:0.23)
Group 2 <i>n</i> = 3	<i>n</i> = 39	<i>n</i> = 0	<i>n</i> = 0	0
Sections: 39				

64.3 J cm⁻¹ in group 1 (bare fibre) versus 60.2 J cm⁻¹ in group 2 (not statistically different).

A temperature increase around the treated vein (in the tumescent liquid) was observed during fibre pullback. On average, the maximum temperature was 50 °C (min: 32.3 °C; max: 68.3 °C) without using the catheter and 47 °C (min: 34.1 °C; max: 80 °C) using the tulip catheter. These differences were not statistically significant (*p* > 0.05).

Six veins were removed immediately after treatment (Table 1). In three of them, the new tulip catheter was used (group 2). In both the groups, 39 sections were taken for histological analysis.

In the veins treated without the tulip catheter (group 1), an uneven destruction of the vein wall was seen, with ulceration and perforation. Very limited perivenous tissue destruction was seen at the point of perforation. Carbonisation was found at the point of direct contact (Fig. 4). Veins treated using the tulip catheter (group 2) did not show any ulceration or perforation. The vein wall looked normal. Only a limited amount of carbonisation was found intraluminally. The intraluminal blood was denatured probably due to boiling. No perivenous tissue destruction was seen. The extent of ulceration and perforation was significantly different between the two groups.

Veins harvested 10 days after treatment (*n* = 8)(Table 2) showed, in both the groups, a cell-rich necro-inflammatory process surrounding the treated vein. This newly

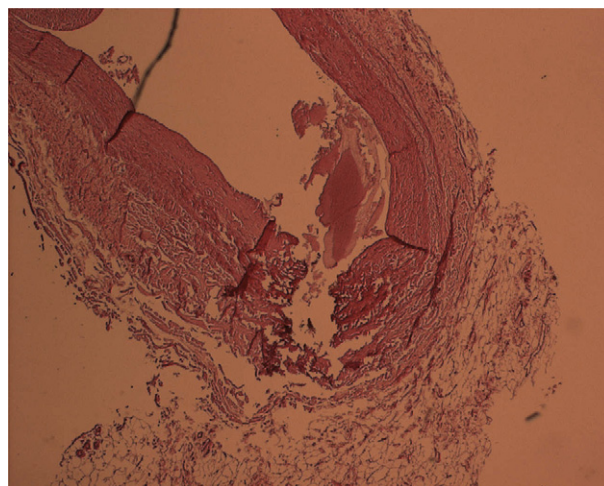


Figure 4 Vein treated without catheter showing ulcerations and carbonisation at the point of direct contact.

Table 2 Histological data of veins harvested 10 days after treatment. Group 1: without catheter. Group 2: with tulip-catheter.

	none	ulceration	perforation	depth	Circumferential destruction	PVDS
Group 1 <i>n</i> = 4 Sections: 44	<i>n</i> = 19	<i>n</i> = 11	<i>n</i> = 14	0.5 SD: 0.35	64% SD: 24	3.8 SD: 2.1
Group 2 <i>n</i> = 4 Sections: 55	<i>n</i> = 53	<i>n</i> = 2	<i>n</i> = 0	0.02 SD: 0.07	80% SD: 26	1.7 SD: 1.9

PVDS: perivenous tissue destruction scale.

formed inflammatory tissue showed formation of new small vessels with migration of fibroblasts and phagocytes. The destruction of the vein wall was far more extensive than was seen in the sections of the veins removed immediately after treatment: major parts of the vein wall were destroyed and the muscle cells were necrotic (Fig. 5). Perivenous tissue destruction could be seen and

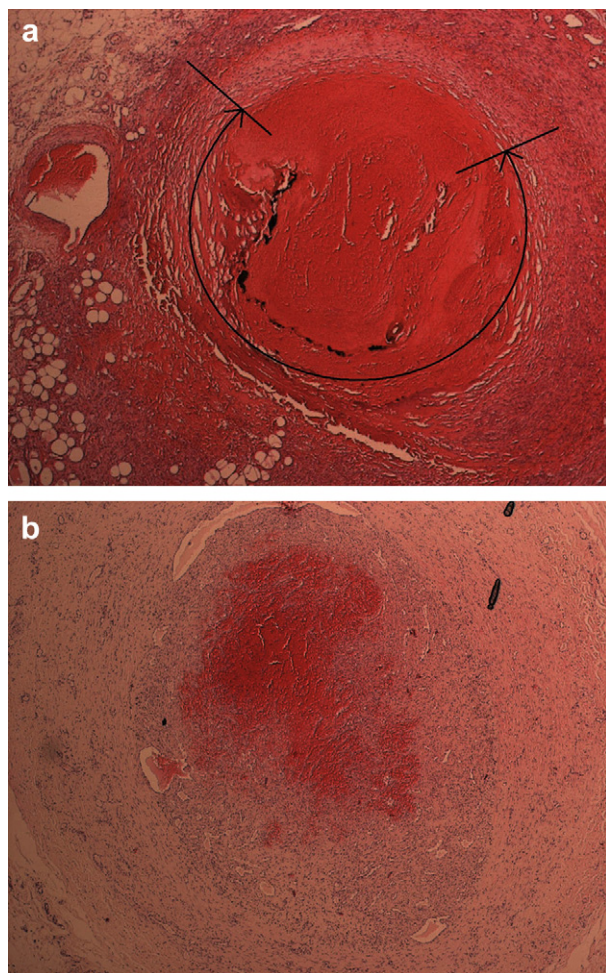


Figure 5 Veins harvested 10 days after treatment. a: Vein treated without catheter showing an ulcer with perivenous tissue destruction especially at the point of direct contact (ulcer). The transmural vein wall necrosis takes 67% of the total circumference (arrow). b: Vein treated using tulip catheter showing a more circumferential vein wall destruction. Notice the infiltration of the vein wall by macrophages and necro-inflammatory cells.

Table 3 Histological data of veins harvested 3 weeks after treatment. Group 1: without catheter. Group 2: with tulip-catheter.

	Circumferential destruction	PVDS
Group 1 <i>n</i> = 3 sections: 43	79% SD: 28	2.1 SD: 2.1
Group 2 <i>n</i> = 3 sections: 45	98% SD: 8.7	2.0 SD: 1.9

PVDS: perivenous tissue destruction scale.

this especially at the points of direct contact between the fibre and the vein wall.

The use of the tulip catheter almost completely eliminated ulceration and perforation after EVLA.

Transmural destruction of the vein wall, with complete necrosis of the muscle cells, is expressed as a percentage of the total circumference of the vein wall. We found, on average, 64% (SD: 24) and 80% (SD: 26) circumferential vein wall necrosis, respectively ($p = 0.02$). The mean perivenous destruction score was of 3.8 (SD: 2.1) in the bare fibre group versus 1.7 (SD: 1.8) for the tulip catheter group ($p = 0.01$).

Three weeks postoperatively (Table 3), six veins were harvested. Organisation in and around the vein walls was very extensive. The inflammatory tissue was infiltrating the treated veins. Newly formed small vessels around the treated veins were accompanied by macrophages and histiocytes, removing the destroyed tissue and forming scar tissue. At the points of perforation in the vein wall, there was deeper destruction of the perivenous tissue (Fig. 6). At these points, we found more carbonisation, which in some cases was encapsulated by polynuclear leucocytes. This perivenous tissue destruction in some cases was clearly in regression due to the healing process. The intraluminal content was mostly damaged with eosinophilic denaturation of the intravascular material. Major parts of the vein wall were destroyed and the muscle cells were necrotic, but sometimes in an uneven distribution. Some parts were not destroyed or incompletely destroyed; the remaining vein wall encapsulated the destroyed part by forming a new endothelial layer on the opposite side, forming a new lumen which might lead to recanalisation (Fig. 7). The exact border of the ulceration was often difficult to establish. More complete circumferential destruction was observed in the tulip catheter group (Table 3). There was no significant difference in measurements of perivenous destruction. In some cases, we found regression of perivenous inflammation due to the healing process and formation of scar tissue.

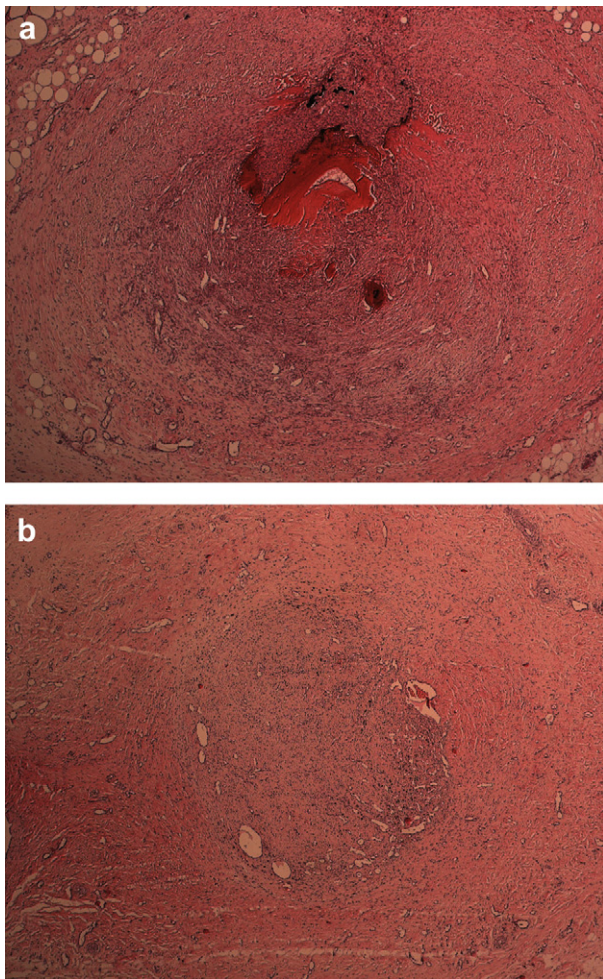


Figure 6 Veins removed three weeks after treatment. a: Vein treated without catheter showing a complete circumferential vein wall destruction. Carbonisation at the point of direct contact. b: Vein treated using the tulip catheter. Complete circumferential vein wall necrosis.

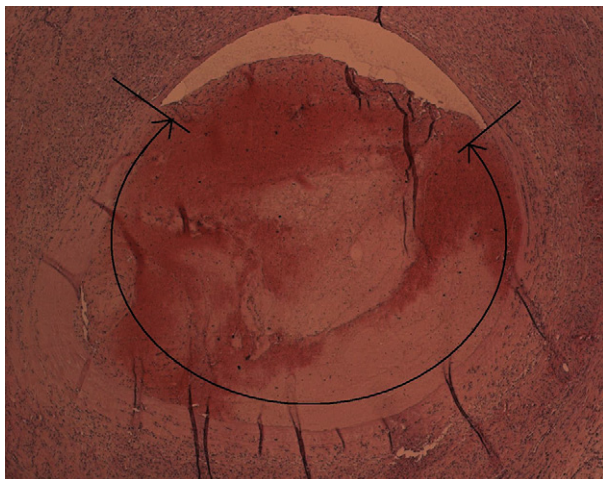


Figure 7 Vein removed three weeks (without catheter) after treatment showing a recanalisation at a point where the vein wall has not been sufficiently destroyed. Circumferential vein wall destruction takes 70% (arrow).

Discussion

EVLA of the incompetent saphenous vein is safe and is at least as effective as surgery.¹⁻⁵ Complications include postoperative ecchymosis, pain and periphlebitis, and recanalisation may occur in incompletely treated veins.^{8,18,19} By centring the fibre intraluminally and avoiding direct contact between the fibre tip and the vein wall, we examined whether morphological causes of postoperative complications could be prevented. The tulip catheter minimised ulceration and perforation of the vein wall. Veins removed immediately after treatment showed no perforation and only infrequent ulceration when the tulip catheter was used. The vein wall appeared to be untouched. We believe that prevention of vein wall perforation will lead to less postoperative ecchymosis.

Veins removed 10 days after treatment showed greater circumferential vein wall destruction compared with the group in which the bare fibre was used. This proves that the direct contact between the fibre and the vein wall is not the most significant mode of action of EVLA. In fact, direct contact is responsible for the ulceration and perforation due to the convection of heat energy from the fibre tip into the surrounding tissue^{7,13} and should be avoided if possible. Energy leakage through the perforations is responsible for perivenous tissue destruction and inflammation.⁷ We found greater perivenous tissue destruction score with the bare fibre. However, the temperature rise in the perivenous fluid did not differ significantly in the two groups, but there was a wide range of measurement. This is probably due to the position of the thermocouple. If the needle is positioned very near the vein wall a large temperature rise was found, but if the needle tip was positioned some millimetres away from the vein wall the temperature rise was much more limited.

The extent of vein wall destruction and perivenous tissue destruction cannot be assessed in veins harvested immediately after treatment, but only in samples removed later.⁷ Absorption is the primary event that allows a laser or other light source to cause a potentially therapeutic (or damaging) effect on a tissue. If the temperature rises above 42 °C, protein denaturation starts. Due to the transformation of light energy into thermal energy, the temperature in and around the treated veins rises.^{20,21} The vein wall cells are heated and their intracellular proteins denature and the cells become necrotic. This cannot be detected histologically until sufficient time has elapsed to allow inflammatory and tissue repair processes to begin.

Three weeks postoperatively, vein wall destruction is even more extensive and the organisation of destroyed tissue into scar tissue becomes very clear. The perivenous inflammatory tissue is in regression and the perivenous tissue destruction is more demarcated in both the groups. Necrotic cells have been eliminated by the inflammatory cells and the macrophages and fibrotic tissue is formed. So the advantage in using the tulip catheter in reducing the perivenous tissue destruction and the secondary appearance of inflammatory tissue is time limited. The appearance of the perivenous

inflammation may correlate with the clinically found 'periphlebitis'. This is a common complication of EVLA and is defined as a burning sensation around the treated vein. It usually starts on the fifth postoperative day. Its intensity and duration are variable, and this uncomfortable burning sensation improves with the intake of anti-inflammatory drugs.

In some veins, we found the formation of a new lumen when the vein wall had been partially destroyed. On the opposite side of the vein a new endothelial layer was formed, and this could result in recanalisation. It is not known whether this segmental formation of a new lumen clinically will result in a recanalisation, but if major parts of the vein wall remain undamaged it is likely. Since the use of the tulip catheter results in more even vein wall destruction, a higher occlusion rate might be expected.

The lateral saphenous vein in goats has been used as a venous model in the previous work in this field.^{7,22} These are not varicose veins and the thickness of the vein wall is therefore somewhat smaller than that of human varicose veins. Whilst this is a useful model it does not replicate human varicose saphenous veins.

Conclusion

EVLA using a new tulip-shaped, self-expandable catheter fixed to the fibre minimises ulceration and perforation in the treated vein. It also results in a more even circumferential vein wall necrosis and less perivenous tissue destruction. We believe that this may result in less postoperative ecchymosis, pain, periphlebitis and possibly a higher occlusion rate when used for the management of varicose veins. These hypotheses require investigation in clinical studies.

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There is no conflict of interests. Tobrix manufactured the tulip device and delivered it for free.

References

- 1 van den Bos R, Arends L, Kockaert M, Neumann M, Nijsten T. Endovenous therapies of lower extremity varicosities are at least as effective as surgical stripping or foam sclerotherapy: meta-analysis and meta-regression of case series and randomized clinical trials. *J Vasc Surg* 2009;**49**(1):230–9.
- 2 Rasmussen LH, Bjoern L, Lawaetz M, Blemings A, Lawaetz B, Eklof B. Randomized trial comparing endovenous laser ablation of the great saphenous vein with high ligation and stripping in patients with varicose veins: short-term results. *J Vasc Surg* 2007;**46**(2):308–15. Epub 2007 Jun 27.
- 3 Kalteis M, Berger I, Messie-Werndl S, Pistrich R, Schimetta W, Pölz W, et al. High ligation combined with stripping and endovenous laser ablation of the great saphenous vein: early results of a randomized controlled study. *J Vasc Surg* 2008;**47**(4):822–9. discussion 829. Epub 2008 Mar 4.
- 4 Darwood RJ, Theivacumar N, Dellagrammaticas D, Mavor AI, Gough MJ. Randomized clinical trial comparing endovenous laser ablation with surgery for the treatment of primary great saphenous varicose veins. *Br J Surg* 2008;**95**(3):294–301.
- 5 Vuylsteke M, Van Den Bussche D, Audenaert EA, Lissens P. Endovenous laser obliteration for the treatment of primary varicose veins. *Phlebology* 2006;Vol. 21(nr 2):80–7.
- 6 Schmedt CG, Sroka R, Steckmeier S, Meissner OA, Babaryka G, Hunger K, Ruppert V, Sadeghi-Azandarayani M, Steckmeier BM. Investigation on radiofrequency and laser (980 nm) effects after endoluminal treatment of saphenous vein insufficiency in an ex-vivo model. *Eur J Vasc Endovasc Surg* 2006;**32**:318–25.
- 7 Vuylsteke M, Vondorp J, Roelens J, De Bo Th, Mordon S. Endovenous laser treatment: a morphological study in an animal model. *Phlebology* (publication in process).
- 8 Vuylsteke M, Liekens K, Moons P, Mordon S. Endovenous laser treatment of saphenous vein reflux: how much energy do we need to prevent recanalizations? *Vasc Endovascular Surg* 2008;**42**(2):141–9.
- 9 Proebstle TM, Sandhofer M, Kargl A, Gül D, Rother W, Knop J, Lehr HA. Thermal damage of the inner vein wall during endovenous laser treatment: key role of energy absorption by intravascular blood. *Dermatol Surg* 2002;**28**(7):596–600.
- 10 Kaspar S, Siller J, Cervinkova Z, Danet T. Standardisation of parameters during endovenous therapy of truncal varicose veins-experimental ex-vivo study. *Eur J Vasc Endovasc Surg* 2007;**34**(2):224–8.
- 11 Corcos L, De Anna D, Dini S, De Anna D, Marangoni O, Ferlaino E, Procacci T, Spina T, Dini M. The immediate effects of endovenous diode 808nm laser in the greater saphenous vein: morphologic study and clinical implications. *J Vasc Surg* 2005;**41**(6):1018–24.
- 12 Fan CM, Rox-Anderson R. Endovenous laser ablation: mechanism of action. *Phlebology* 2008;**23**(5):206–13.
- 13 Disselhof BCM, Rem AI, Verdaasdonk RM, Kinderen DJ, Moll FL. Endovenous laser ablation: an experimental study on the mechanism of action. *Phlebology* 2008;**23**:69–76.
- 14 van der Veght AK, Govaert LE; Polymeren, van keten tot kunststof. ISBN 90-407-2388-5.
- 15 Molinaro Hope. Flowmeter components use PEEK polymer. *Plastic Engineering*; 2004.
- 16 Murphy J. PEEK meets needs for high-frequency surgery. High performance plastics. 1998. HighBeam Research. *International Newsletters* 2009;**23**.
- 17 Proebstle TM, Moehler T, Herdemann S. Reduced recanalization rates of the great saphenous vein after endovenous laser treatment with increased energy dosing: definition of a threshold for the endovenous fluence equivalent. *J Vasc Surg* 2006 Oct;**44**(4):834–9.
- 18 Proebstle TM, Krummenauer F, Gul D, Knop J. Non-occlusion and early reopening of the saphenous vein after endovenous laser treatment is fluence dependent. *Dermatol Surg* 2004;**30**:174–8.
- 19 Timperman PE, Sichlau M, Ryu RK. Greater energy delivery improves treatment success of endovenous laser treatment of incompetent saphenous veins. *J Vasc Interv Radiol* 2004;**15**:1061–3.
- 20 Zimmet SE, Min RJ. Temperature changes in perivenous tissue during endovenous laser treatment in a swine model. *J Vasc Interv Radiol* 2003;**14**:911–5.
- 21 Vlarengo LMA, Poterio-Filho J, Poterio GMB, Menezes FH, Meirelles GV. Endovenous laser treatment for varicose veins in patients with active ulcers: measurement of intravenous and perivenous temperatures during the procedure. *Dermatol Surg* 2007;**33**:1234–42.
- 22 Parente EJ, Rosenblatt M. Endovenous laser treatment to promote venous occlusion. *Lasers Surg Med* 2003;**33**(2):115–8.